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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: George D. Hartman et al.



Serial No. 10/533,028

Filed: April 26, 2005

For: KINASE INHIBITORS

Art Unit: To Be AssignedExaminer: To Be Assigned

Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

**INFORMATION DISCLOSURE STATEMENT  
UNDER 37 CFR 1.97**

Sir:

1. In compliance with 37 C.F.R. 1.97, submitted on the attached form herewith is a list of patents, publications or other information which are requested to be made of record in this application. This Information Disclosure Statement is not an admission that any patent, publication or other information referred to herein is "prior art" for this invention.

In accordance with 37 C.F.R. 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. 1.56(b).

2. In accordance with 37 C.F.R. 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made.

3. Applicants respectfully request that the Examiner initial the attached form after reviewing the pertinence of each reference.

4. Pursuant to 37 C.F.R. 1.98 (a)(2)(ii), copies of each cited U.S. patent and each U.S. patent application publication are not enclosed herewith.

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MERCK &amp; CO., INC.

By 

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5. Pursuant to 37 C.F.R. 1.98(d), copies of references listed on the attached form that were submitted to or cited by the Office in a related application upon which the instant application relies for an earlier filing date under 35 U.S.C. 120 are not enclosed. Related application(s) in which references were submitted to or cited by the Office are as follows:

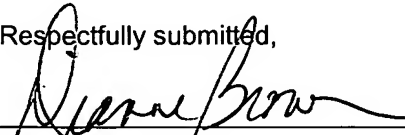
RELATED APPLICATION		
U. S. SERIAL NUMBER	FILING DATE	MERCK CASE

If this is inconvenient, additional copies will be submitted upon request.

6. In accordance with 37 C.F.R. 1.97, (check one)

- ☐ the attached information is filed within three months of the filing date of the captioned case.
- ☒ the attached information is filed more than three months after the filing date but prior to the mailing of a first Office Action on the merits.
- ☐ the attached information is filed before the mailing of a first Office action after the filing of a request for continued examination under §1.114.
- ☐ the attached information is being filed more than three months after the filing date and after the mailing of a first Office Action on the merits, but before the mailing date of a Final Action, Notice of Allowance, or an action that otherwise closes prosecution in the application. The enclosed authorization is therefore given to charge Deposit Account No. 13-2755 for the fee required under 37 C.F.R. 1.17(p).
- ☐ each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Statement.
- ☐ each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart application *and this communication was not received by any individual designated in §1.56(c) more than thirty days prior to the filing of the information disclosure statement.*
- ☐ no item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, was known to any individual designated under 37 C.F.R. 1.56(c) more than three months prior to the filing of this Statement.

Respectfully submitted,

  
 By: Dianne Brown  
 Attorney                      For Applicant(s)

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MERCK & CO., INC.

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Date: October 17, 2005

[illegible][illegible]

Examiner Signature		Date Considered	
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Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

SEND TO: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450. Computer generated form "IDS Form" (IDS Folder), Merck & Co., Inc., -7/12/2005

Substitute for form 1449B/PTO <b>INFORMATION DISCLOSURE</b>  <b>STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>				<b>COMPLETE IF KNOWN</b>	
				Application Number	10/533,028
				Filing Date	April 26, 2005
				First Named Inventor	George D. Hartman
				Group Art Unit	To Be Assigned
				Examiner Name	To Be Assigned
Sheet	2	of	3	Attorney Docket Number	20942P

NON PATENT LITERATURE DOCUMENTS		
Examiner Initials*	Cite No.	Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.
	3	Amirkhosravi, A., et. al., "Blockade of GpIIb/IIIa inhibits the release of vascular endothelial growth factor (VEGF) from tumor cell-activated platelets and experimental metastasis", Platelets, 10, pp. 285-292 (1999)
	4	Brockelsby, J., et al., "VEGF Via VEGF Receptor-1 (Flt-1) Mimics preeclamptic Plasma in Inhibiting Uterine Blood Vessel Relaxation in Pregnancy: Implications in the Pathogenesis of Preeclampsia", Laboratory Investigation, 79, pp. 1101-1111 (1999)
	5	Carlson, B.A., et al., "Flavopiridol Induces G1 Arrest with Inhibition of Cyclin-dependent Kinase (CDK) 2 and CDK2 in Human Breast Carcinoma Cells", Cancer Research, 56, pp. 2973-2978 (1996)
	6	Deckers, M.M.L., et al., "Expression of Vascular Endothelial Growth Factors and Their Receptors during Osteoblast Differentiation", Endocrinology, 141, pp. 1667-1674 (2000)
	7	Detmar, M., "The role of VEGF and thrombospondins in skin angiogenesis", Journal of Dermatological Science, 24, Suppl. (1), pp. S78-S84 (2000)
	8	Dickinson, A.J., et al., "Quantification of angiogenesis as an independent predictor of prognosis in invasive bladder carcinomas", British Journal of Urology, 74, pp. 762-766 (1994)
	9	Ellis, L.M., et al., "Down-regulation of vascular endothelial growth factor in human colon carcinoma cell lines by antisense transfection decreases endothelial cell proliferation", Surgery, 120, (5), pp. 871-878 (1996)
	10	Gasparini, G. and Harris, A.L., "Clinical Importance of the Determination of Tumor Angiogenesis in Breast Carcinoma: Much More Than a New Prognostic Tool", Journal of Clinical Oncology, 13, pp. 765-782 (1995)
	11	Gerber, et al., "VEGF couples hypertrophic cartilage remodeling, ossification and angiogenesis during endochondral bone formation", Nature Medicine, Vol. 5, (6), pp. 623-628 (1999)
	12	Giatromanolaki, A., et al., "The angiogenic pathway 'vascular endothelial growth factor/flk-I(KDR)-receptor' in rheumatoid arthritis and osteoarthritis", Journal of Pathology, 194, pp. 101-108 (2001)
	13	Glab, N., et al., "Olomoucine, an inhibitor of the cdc2/cdk2 kinases activity, blocks plant cells at the G1 to S and G2 to M cell cycle transitions", FEBS Letters, 353, pp. 207-211 (1994)
	14	Greenberg, D.A., "Angiogenesis and Stroke", Drug News Perspect, 11, pp. 265-270 (1998)
	15	Gunningham, S.P., et al., "Vascular Endothelial Growth Factor-B and Vascular Endothelial Growth Factor-C Expression in Renal Cell Carcinomas: Regulation by the von Hippel-Lindau Gene and Hypoxia", Cancer Research, 61, pp. 3206-3211 (2001)
	16	Hasegawa, T., et al., "Intracortical osteoblastic osteosarcoma with oncogenic rickets", Skeletal Radiology, 28, pp. 41-45 (1999)
	17	Jain, R.K., "Normalizing tumor vasculature with anti-angiogenic therapy: A new paradigm for combination therapy", Nature Medicine, Vol. 7, (9), pp. 987-989 (2001)

Examiner Signature		Date Considered	
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	18	Kelland, L.R., "Flavopiridol, the first cyclin-dependent kinase inhibitor to enter the clinic: current status", Expert Opinion on Investigational Drugs, 9, pp. 2903-2911 (2000)
	19	Kitagawa, M., et al., "Butyrolactone I, a selective inhibitor of cdk2 and cdc2 kinase", Oncogene, 8, pp. 2425-2432 (1993)
	20	Levis, M., et al., "A FLT3 tyrosine kinase inhibitor is selectively cytotoxic to acute myeloid leukemia blasts harboring FLT3 internal tandem duplication mutations", Blood, Vol. 98 (3), pp. 885-887 (2001)
	21	Losiewicz, M.D., et al., "Potent Inhibition of CDC2 Kinase Activity By The Flavonoid L86-8275", Biochemical and Biophysical Research Communications, 201, pp. 589-595 (1994)
	22	Nakagawa, M., et al., "Vascular endothelial growth factor (VEGF) directly enhances osteoclastic bone resorption and survival of mature osteoclasts", FEBS Letters, 473, pp. 161-164 (2000)
	23	Paul, R., et al., "Src deficiency or blockade of Src activity in mice provides cerebral protection following stroke", Nature Medicine, 7, pp. 222-227 (2001)
	24	Rak, J., et al., "Mutant ras Oncogenes Upregulate VEGF/VPF Expression: Implications for Induction and Inhibition of Tumor Angiogenesis", Cancer Research, 55, pp. 4575-4580 (1995)
	25	Senderowicz, A.M., "Flavopiridol: the first cyclin-dependent kinase inhibitor in human clinical trials", Investigational New Drugs, 17, pp. 313-320 (1999)
	26	Smith, Stephen K., "Regulation of angiogenesis in the endometrium", Trends in Endocrinology & Metabolism, Vol. 12, (4), pp. 147-151 (2001)
	27	Toi, M., et al., " Association of Vascular Endothelial Growth Factor Expression with Tumor Angiogenesis and with Early Relapse in Primary Breast Cancer", Japan. J. Cancer Res., 85, pp. 1045-1049 (1994)
	28	van der Flier et al., "Vascular Endothelial Growth Factor in Bacterial Meningitis: Detection in Cerebrospinal Fluid and Localization in Postmortem Brain", J. Infectious Diseases, 183, pp. 149-153 (2001)
	29	Williams, J.K., et al., "Tumor Angiogenesis as a Prognostic Factor in Oral Cavity Tumors", American Journal of Surgery, 168, pp. 373-380 (1994)

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